REMARKS

On October 18, 2006 the undersigned attorney received a call from Examiner Balls with regard to the present application and co-pending application 10/534,582. The Examiner explained that while the claims in 10/764,229 were now in condition to be allowed, the Patent office had instituted a new policy, such that the pending claims in 10/764,229 would not be allowed, unless one of two further actions were taken by the applicants. In particular, in order for the Examiner to allow the application, Applicants must either:

1) file a terminal disclaimer in both 10/534,582 and the present application; or
2) cancel, in co-pending application 10/534,582, the subject matter that is in condition to be allowed in the present application 10/764,229.

Applicants have chosen the option 2), and have thus, canceled from co-pending application 10/534,582, the subject matter that is in condition to be allowed in the present application. A copy of the Amendment (styled "Second Preliminary Amendment") is enclosed. Applicants wish to direct the Examiner's attendion to the 12th and 18th species of claim 20 in 10/534,582, which are the cis and trans stereoisomers of the compound of claim 30 in the present application 10/764,229.

Having addresses all of the outstanding objections and rejection, applicants respectfully submit that the application is now in condition for allowance, and passage thereto is earnestly requested. The Examiner is invited to contact the undersigned attorney at the telephone number provided below if such would advance the prosecution of this case.

Respectfully submitted,

By _____
Curtis C. Panzer
Reg. No. 33,752
Attorney for Applicant

MERCK & CO., Inc.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-3199

Date: 24 October 2006

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant :	D. Dube, et al.		
Serial No. :	10/534,582	Case MCO73YP	Art Unit: 1625
Filed :	May 11, 2005		Examiner: Balls, R.
For :	4-OXO-1-(3-SUBSTITUTED PHENYL-1,4-DIHYDRO-1,8-NAPHTHYRIDINE-3-CARBOXAMIDE PHOSPHODIESTERASE-4 INHIBITORS		

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

SECOND PRELIMINARY AMENDMENT

Dear Sir:

Prior to examination in the merits please amend the above captioned application as indicated below. Any additional fees associated with this Amendment may be charged to Merck Deposit Account No. 13-2755.

AMENDMENTS TO THE CLAIMS are reflected in the listing of claims which begins on page 2 of this paper.

REMARKS begin on page 10 of this paper.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date appearing below.

MERCK & CO., INC.

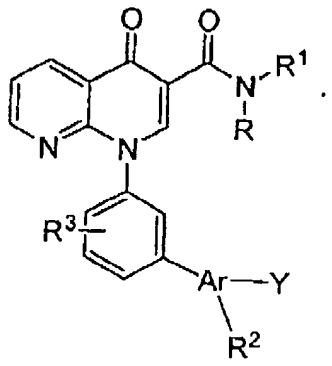
By _____ Date 10-24-2006

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listing of claims in the application.

1. (Canceled)

2. (Presently amended) A compound represented by Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein

Ar is phenyl, pyridyl, pyrimidyl, indolyl, quinolinyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiadiazolyl, or imidazolyl; or oxides thereof when Ar is a heteroaryl;

Y is –COOH, or -C_{1-6}alkyl(C_{1-4}alkyl)$_n$–COOH, ~~-C_{3-4}cycloalkyl(C_{1-4}alkyl)$_m$-COOH~~, wherein the -C_{1-6}alkyl ~~and the C_{3-4}cycloalkyl~~ is optionally substituted with halogen, alkoxy, hydroxy or nitrile, and the (C_{1-4}alkyl) substituents are optionally linked to form a C_{3-4}cycloalkyl ; wherein n is 0, 1, 2, 3 or ~~4, m is 0, 1 or 2~~;

R is H or –C_{1-6}alkyl;

R^1 is H, or –C_{1-6}alkyl, –C_{3-6}cycloalkyl, –C_{1-6}alkoxy, –C_{2-6}alkenyl, –C_{3-6}alkynyl, heteroaryl, or heterocycle group, optionally substituted with 1-3 independent haloC_{1-6}alkyl, -C_{1-6}alkyl, –C_{1-6}alkoxy, OH, amino, –(C_{0-6}alkyl)–SO_p–(C_{1-6}alkyl), nitro, CN, =N-O-C_{1-6}alkyl, -O-N=C_{1-6}alkyl, or halogen substituents, wherein p is 0, 1 or 2;

R^2 is H, halogen,-CN, -NO_2, –C_{1-6}alkyl, –C_{3-6}cycloalkyl, -O- C_{3-6}cycloalkyl, O-C_{1-6}alkyl, O-C_{3-6}cycloalkyl-C_{1-6}alkyl(C_{3-6}cycloalkyl)(C_{3-6}cycloalkyl), –C_{1-6}alkoxy, phenyl, heteroaryl, heterocycle, amino, –C(O)–C_{1-6}alkyl, –C(O)–O–C_{1-6}alkyl, –C_{1-6}alkyl(=N-OH), -C(N=NOH)C_{1-6}alkyl, –C_{0-6}alkyl(oxy)C_{1-6}alkyl-phenyl, –SO_kNH(C_{0-6}alkyl), or -(C_{0-6}alkyl)–SO_k–(C_{1-6}alkyl), wherein the phenyl, heteroaryl or heterocycle is optionally substituted with halogen, -C_{1-6}alkyl, –C_{1-6}alkoxy, hydroxy, amino,

or -C(O)-O-C_{1-6}alkyl, and wherein the alkyl or cycloalkyl is optionally substituted with 1-6 independently selected halogens or –OH, and wherein k is 0, 1, or 2;

R^3 is selected from H, halogen, CN, -C_{1-6}alkyl, -C_{3-6}cycloalkyl, nitro, -C(O)-C_{1-6}alkyl, -C(O)-O-C_{0-6}alkyl, -$SO_{n'}$NH(C_{0-6}alkyl), or -(C_{0-6}alkyl)-$SO_{n'}$-(C_{1-6}alkyl), O-C_{1-6}alkyl, O-C_{3-6}cycloalkyl, wherein n' is 0, 1, or 2 and wherein the alkyl and cycloalkyl is optionally substituted with 1-6 independently selected halogen or OH.

3 to 10. (Canceled)

11. (Original) The compound according to claim 2, or a pharmaceutically acceptable salt, wherein

Ar is pyridyl, pyrimidyl, or oxide thereof.

12. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt, wherein

R^1 is –C_{1-6}alkyl optionally substituted with 1-3 independent -C_{1-6}alkyl, –C_{1-6}alkoxy, OH, amino, –(C_{0-6}alkyl)–SO_p–(C_{1-6}alkyl), nitro, CN, =N-O-C_{1-6}alkyl, -O-N=C_{1-6}alkyl, or halogen substituents.

13. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R^1 is –C_{3-6}cycloalkyl optionally substituted with 1-3 independent -C_{1-6}alkyl, –C_{1-6}alkoxy, OH, amino, –(C_{0-6}alkyl)–SO_p–(C_{1-6}alkyl), nitro, CN, =N-O-C_{1-6}alkyl, -O-N=C_{1-6}alkyl, or halogen substituents.

14. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R is hydrogen.

15. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R^2 is hydrogen or .–C_{1-3}alkyl or halogen.

16. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R^1 is –C_{3-6}cycloalkyl optionally substituted with methyl or halo; and

R is hydrogen.

17. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R^1 is cyclopropyl optionally substituted with methyl or halo; and

R and R^2 are hydrogen or halogen;

R^3 is hydrogen or halogen.

18. (Original) The compound according to claim 2, or a pharmaceutically acceptable salt thereof, wherein

R and R^3 are hydrogen,;

R^1 is $-C_{3-6}$cycloalkyl optionally substituted with methyl or halo, or $-C_{1-3}$alkyl optionally substituted with 1-3 halo; and

Ar is phenyl.

19. (Canceled)

20. (Original) The compound ~~according to claim 2,~~ which is

2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-3-yl}cyclopropanecarboxylic acid;

2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-3-yl}-2-methylpropanoic acid;

2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-2-methylpropanoic acid;

3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-3-methylbutanoic acid;

{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}(hydroxy)acetic acid;

1-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(cis)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

5-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-2,2-dimethyl-1,3-dioxolane-4-carboxylic acid;

1-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-3-yl}cyclopropanecarboxylic acid;

1-cyano-3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-2,2-dimethylcyclopropanecarboxylic acid;

2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-3-fluoro-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

(cis)-2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-3-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-bromo-5'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-3-methyl-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-2-methyl-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3-chloro-3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(cis)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-3-fluoro-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-carboxylic acid;

2-(trans)-{3'-[3-(morpholin-4-ylcarbonyl)-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[4-oxo-3-({[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]amino}carbonyl)-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-({[2-(methylthio)ethyl]amino}carbonyl)-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-({[2-(methylsulfonyl)ethyl]amino}carbonyl)-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-(5-{3-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]phenyl}thien-2-yl)cyclopropanecarboxylic acid;
2-(trans)-{3'-[3-{[(cyclopropylmethyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;
2-(trans)-{3'-[3-{[(1-cyanocyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid; or
3-{3'-[3-[(isopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-3-methylbutanoic acid.

21. (Presently amended) A compound ~~of claim 1~~ which is

(+)-(trans)-2-{3-fluoro-3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;
1-({3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}methyl)cyclobutanecarboxylic acid;
(trans)-2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-2-methylcyclopropanecarboxylic acid;
(trans)-2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-2-yl}cyclopropanecarboxylic acid;
3-methyl-3-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}butanoic acid;
(trans)-2-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-2-yl}cyclopropanecarboxylic acid;
(trans)-2-{3'-[4-oxo-3-{[(2,2,3,3,3-pentafluoropropyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;
(trans)-2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-1-fluorocyclopropanecarboxylic acid;
(+)-(trans)-2-{3-chloro-3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;
(-)-(trans)-2-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-ethyl 2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylate;

(+)-(trans)-isopropyl 2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylate;

tert-butyl 3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-2,2-dimethylpropanoate;

3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-2,2-dimethylpropanoic acid;

3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-3-yl}-2,2-dimethylpropanoic acid;

1-({3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-3-yl}methyl)cyclobutanecarboxylic acid;

3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-2-yl}-2,2-dimethylpropanoic acid;

1-({3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-2-yl}methyl)cyclobutanecarboxylic acid;

(+)-(trans)-2-{3'-[3-[(*tert*-butylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-2-{3'-[3-[(cyclobutylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}bicyclo[1.1.1]pentane-1-carboxylic acid;

4-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-4-hydroxypentanoic acid;

(trans)-2-{3'-[3-{[(□)-cis-(2-fluorocyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-(+)-biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-2-{3'-[3-{[(dicyclopropylmethyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

4-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-2,2-dimethylbutanoic acid;

(+)-(trans)-2-{3'-[3-{[(1-hydroxycyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-2-{3'-[4-oxo-3-{[(1-phenylcyclopropyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

4-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-3,3-dimethylbutanoic acid;

(+)-(trans)-2-{3'-[3-{[(1-cyclopropyl-1-methylethyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

1-({3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}methyl)cyclobutanecarboxylic acid;

(+)-(trans)-2-{3'-[3-{[(cyclopropylmethyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

(-)-(trans)-2-{3-fluoro-3'-[3-{[(1-hydroxycyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

(trans)-2-{3'-[4-oxo-3-{[((□)-2,2,2-trifluoro-1-methylethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]-(+)-biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-2-{3'-[3-{[(1-methylcyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

2,2-dimethyl-4-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}butanoic acid;

2,2-dimethyl-3-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}propanoic acid;

(-)-(trans)-2-{3-chloro-3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid; or

(+)-(trans)-2-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid.

22. (Presently amended) A pharmaceutical composition comprising

a therapeutically effective amount of the compound according to ~~claim 1~~ claim 2 or a pharmaceutically acceptable salt thereof; and

a pharmaceutically acceptable carrier.

23 to 24. (Canceled).

25. (Presently amended) A method of treatment or prevention of asthma, chronic bronchitis, chronic obstructive pulmonary disease (COPD), eosinophilic granuloma, psoriasis and other benign or malignant proliferative skin diseases, endotoxic shock (and associated conditions such as laminitis and colic in horses), septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, inflammatory arthritis, osteoporosis, chronic glomerulonephritis, atopic dermatitis, urticaria, adult respiratory distress syndrome, infant respiratory distress syndrome, chronic obstructive pulmonary disease in animals, diabetes insipidus, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, arterial restenosis, atherosclerosis, neurogenic inflammation, pain, cough, rheumatoid arthritis, ankylosing spondylitis, transplant rejection and graft versus host disease, hypersecretion of gastric acid, bacterial, fungal or viral induced sepsis or septic shock, inflammation and cytokine-mediated chronic tissue degeneration, osteoarthritis, cancer, cachexia, muscle wasting, depression, memory impairment, monopolar depression, acute and chronic neurodegenerative disorders with inflammatory components, Parkinson disease, Alzheimer's disease, spinal cord trauma, head injury, multiple sclerosis, tumour growth and cancerous invasion of normal tissues comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to ~~claim 1~~ claim 2 or a pharmaceutically acceptable salt thereof.

26. (Presently amended) A method of enhancing cognition in a healthy subject comprising administering a safe cognition enhancing amount of compound according to ~~claim 1~~ claim 2, or a parmaceutically salt thereof.

27 to 34. (Canceled)

REMARKS

Claims 2, 11-18, 20-22, 25 and 26 are pending in this application.

On October 18, 2006 the undersigned attorney received a call from Examiner Balls with regard to the pending application and co-pending application 10/764,229. The Examiner explained that while the claims in 10/764,229 were now in condition to be allowed, the Patent Office had instituted a new policy, such that the pending claims in 10/764,229 would not be allowed, unless one of two further actions were taken by the applicants. In particular, in order for the Examiner to allow the application, Applicants must either:

1) file a terminal disclaimer in both 10/764,229 and the present application; or

2) cancel, in the present unexamined application, the subject matter that is in condition to be allowed in co-pending application 10/764,229.

Applicants have chosen the option 2), and have thus, canceled from the present application the subject matter that is in condition to be allowed in co-pending application 10/764,229. Applicants wish to direct the Examiner's attendion to the 12th and 18th species of claim 20 in the present application, which are the cis and trans stereo isomers of the compound of claim 30 in co-pending application 10/764,229.

Applicants point out that in complying with the Examiner's requirement, they believe they have been over inclusive in what has been canceled from the present application. That is, applicants have canceled more than what is in condition for allowance in co-pending 10/764,229. Applicants reserve the right to prosecute such subject matter in a continuing or divisional application.

U.S.S.N.
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PAGE NO. 11

Applicants believe that this amendment satisfies the examiner's concern with regard to allowing 10/764,229. Applicants respectfuilly request early examination of this application. The Examiner is invited to contact the undersigned attorney at the telephone number provided below, if such would advance the prosection of the case.

Respectfully submitted,

By Curtis C Panzer

Curtis C. Panzer
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Date: October 24, 2006